COX-2 Selective (includes Bextra, Celebrex, and Vioxx) and Non-Selective Non-Steroidal Anti-Inflammatory Drugs (NSAIDs)

The Food and Drug Administration (FDA) has issued supplemental request letters to sponsors of all non-steroidal anti-inflammatory drugs (NSAID) requesting that they make labeling changes to their products. These letters include recommended proposed labeling for both the prescription and over-the-counter (OTC) NSAIDs and a medication guide for the entire class of prescription products. All sponsors of marketed prescription Non-Steroidal Anti-Inflammatory Drugs (NSAIDs), including Celebrex (celecoxib), a COX-2 selective NSAID, have been asked to revise the labeling (package insert) for their products to include a boxed warning, highlighting the potential for increased risk of cardiovascular (CV) events and the well described, serious, potential life-threatening gastrointestinal (GI) bleeding associated with their use. The Celebrex labeling will, in addition to the general labeling that will apply to all NSAIDs, also contain safety data from long-term treatment trials with celecoxib.

Manufacturers of **non-prescription** (over-the-counter) NSAIDs are being asked to revise their labeling to provide more specific information about the potential CV and GI risks of their individual products and remind patients of the limited dose and duration of treatment of these products in accordance with the package instructions

In making these decisions, the Center for Drug Evaluation and Research (CDER) considered the risk/benefit profile for each of the drugs. Also considered was;

- review of the regulatory histories and new drug application (NDA) databases of the various NSAIDs,
- FDA and sponsor background documents prepared for the joint Advisory Committee meeting of FDA's Arthritis and Drug Safety and Risk Management Advisory Committees, held February 16-18, 2005,
- all materials and data submitted by other stakeholders to the Advisory Committee meeting, presentations made at the joint meeting
- the specific votes and recommendations made by the joint Committee.

Further information regarding the decisions being announced and specific details regarding the individual products can be found within the documents posted to this Web page.

- Public Health Advisory
- FDA Press Release
- Questions and Answers

- Decision Memo - Analysis and Recommendations for Agency Action - COX-2 Selective and Non-selective NSAIDs (Issued 4/6/2005, posted 4/15/2005)
- COX-2 Selective Drugs (including Bextra, Celebrex, and Vioxx)
- Prescription NSAID Products (6/15/2005)
  - Supplemental Request Letter
  - Labeling Template
  - Medication Guide [PDF] [HTML]
- Over-the-Counter NSAID Products
  - **New** Over-the-Counter (OTC) Nonsteriodal Anti-Inflammatory Drug (NSAID) Products.
    - July 15, 2005. The agency has issued new supplemental labeling request letters for OTC NSAID products. The Agency received comments from industry regarding the June 14th supplemental labeling request letter and labeling template. Upon completion of our review of the comments, the Agency has decided to make revisions to the OTC labeling template and issue a new supplemental labeling request letter.
    - Revised Supplemental Request Letter and Labeling Template (7/18/2005)
  - Supplemental Request Letter and Labeling Template (6/15/2005)

- COX-2 Selective Non-steroidal Anti-inflammatory Drugs (NSAIDs) and Prescription and Over-the-Counter (OTC) Non-selective NSAIDs Approved Under New Drug Application (NDA) Abbreviated New Drug Application (ANDA) Table of Drug Products

COX-2 Selective Drugs

Bextra (valdecoxib)

Current Information

On April 7, 2005, the Food and Drug Administration (FDA) asked Pfizer to voluntarily remove Bextra (valdecoxib) from the market.

- Healthcare Professional Sheet [PDF] [HTML]

Background Information

- FDA Talk Paper (12/9/2004)
- Questions and Answers: Strengthening Warnings on Bextra (12/9/2004)
- Consumer Information Sheet
- FDA Issues Public Health Advisory Recommending Limited Use of Cox-2 Inhibitors. FDA Talk Paper (12/23/2004)
- Public Health Advisory: Non-Steroidal Anti-Inflammatory Drug Products (NSAIDs) (12/23/2004)

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Celebrex (celecoxib)

Current Information

- Patient Information Sheet [PDF] or [HTML]
- Healthcare Professional Information
  - Healthcare Professional Sheet [PDF] or [HTML]
  - Prescribing Information (Celebrex Label)

Background Information

FDA Alert: 3/2005. Based on emerging information, including preliminary reports from one of several long term National Institutes of Health (NIH) prevention studies, the risk of cardiovascular events (composite endpoint including MI, CVA and death) may be increased in patients receiving Celebrex. FDA will be analyzing all available information from these studies to determine whether additional regulatory action is needed.

- Regulatory History of Celebrex from Drugs@FDA
- FDA Statement on the Halting of a Clinical Trial of the Cox-2 Inhibitor Celebrex (12/17/2004)
- FDA Issues Public Health Advisory Recommending Limited Use of Cox-2 Inhibitors. FDA Talk Paper (12/23/2004)
- Public Health Advisory: Non-Steroidal Anti-Inflammatory Drug Products (NSAIDS) (12/23/2004)

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Vioxx (rofecoxib)

Background Information

Merck & Co., Inc. announced a voluntary withdrawal of Vioxx (rofecoxib) from the U.S. and worldwide market due to safety concerns of an increased risk of cardiovascular events (including heart attack and stroke) in patients on Vioxx. Vioxx is a prescription COX-2 selective, non-steroidal anti-inflammatory drug (NSAID) that was approved by FDA in May 1999 for the relief of the signs and symptoms of osteoarthritis, for the management of acute pain in adults, and for the treatment of menstrual symptoms. Vioxx was later approved for the relief of the signs and symptoms of rheumatoid arthritis in adults and children.

- Statement by Dr. Steven Galson, Acting Director, Center for Drug Evaluation and Research (CDER), Regarding November 18, 2004, Committee on Finance of the U.S. Senate Hearing on Drug Safety and the Worldwide Withdrawal by Merck & Co., Inc., of Vioxx. FDA Statement (11/18/2004)
- Congressional Statement on Vioxx and Drug Safety (Posted 11/18/2004)
- FDA releases a statement on Vioxx and recent allegations, and on the Agency's continued commitment to sound science and peer review. FDA Statement (Posted 11/17/2004)
- Slide Presentation by Sandra Kweder, M.D., November 10, 2004. [HTML] [PowerPoint] (Posted 11/10/2004)
- FDA Acts to Strengthen the Safety Program for Marketed Drugs. FDA Statement

(11/5/2004)
- 9/30/2004 Study Report (Posted 11/2/2004)
- FDA Issues Public Health Advisory on Vioxx as its Manufacturer Voluntarily Withdraws the Product. FDA News (9/30/2004)
- FDA Public Health Advisory: Safety of Vioxx (9/30/2004)
- Vioxx (rofecoxib) Questions and Answers (9/30/2004)

Other Prescription Non-selective NSAIDs

Current Information

- Patient Information Sheet (coming soon)
- Healthcare Professional Information [PDF] [HTML]

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COX-2 Selective Non-steroidal Anti-inflammatory Drugs (NSAIDs) and Prescription and Over-the-Counter (OTC) Non-selective NSAIDs Approved Under New Drug Application (NDA) Abbreviated New Drug Application (ANDA)

COX-2 Selective NSAIDs	
Chemical Name	**Brand Name**
Celecoxib	Celebrex
Valdecoxib	Bextra
Rofecoxib	Vioxx

Non-selective NSAIDs	
Chemical Name	**Brand Name**
Diclofenac	Cataflam, Voltaren, Arthrotec (combination with misoprostol)
Diflunisal	Dolobid
Etodolac	Lodine, Lodine XL
Fenoprofen	Nalfon, Nalfon 200
Flurbiprofen	Ansaid
Ibuprofen**	Motrin, Motrin IB, Motrin Migraine Pain, Advil, Advil Migraine Liqui-gels, Ibu-Tab 200, Medipren, Cap-Profen, Tab-Profen, Profen, Ibuprohm, Children's Elixsure *, Vicoprofen (combination with hydrocodone), Combunox

	(combination with oxycodone)
Indomethacin	Indocin, Indocin SR, Indo-Lemmon, Indomethegan
Ketoprofen**	Oruvail, Orudis, Actron
Ketorolac	Toradol
Mefenamic Acid	Ponstel
Meloxicam	Mobic
Nabumetone	Relafen
Naproxen**	Aleve, Naprosyn, Anaprox, Anaprox DS, EC-Naproxyn, Naprelan, Naprapac (copackaged with lansoprazole)
Oxaprozin	Daypro
Piroxicam	Feldene
Salsalate	Disalcid
Sulindac	Clinoril
Tolmetin	Tolectin, Tolectin DS, Tolectin 600

*There are many OTC Combinations with ibuprofen: Advil Cold And Sinus, Advil Cold, Advil Allergy Sinus, Children's Advil Allergy Sinus, Ibuprohm Cold and Sinus, Sine-Aid IB, Children's Motrin Cold.

**There are over-the-counter versions of these prescription medications.

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